

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

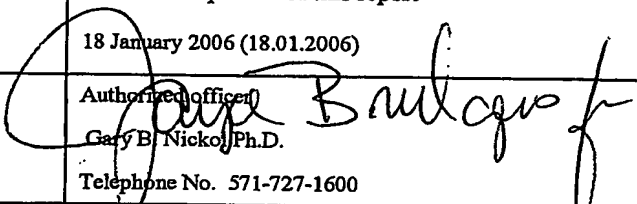
|  |   |   |
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| Applicant's or agent's file reference<br>11245/48976   | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |   |
| International application No.<br>PCT/US04/18451  | International filing date (day/month/year)<br>09 June 2004 (09.06.2004)   | Priority date (day/month/year)<br>09 June 2003 (09.06.2003) |
| International Patent Classification (IPC) or national classification and IPC<br>IPC(7): A61K 39/385, 39/395 and US Cl.: 424/195.11, 178.1, 138.1 |   |   |
| Applicant<br>SAMUEL WAKSAL   |   |   |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.  
  
☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

|  |   |
|--|---|
| Date of submission of the demand<br>11 April 2005 (11.04.2005)   | Date of completion of this report<br>18 January 2006 (18.01.2006)   |
| Name and mailing address of the IPEA/US<br>Mail Stop PCT, Attn: IPBA/ US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (571) 273-3201 | Authorized officer<br><br>Gary B. Nickol, Ph.D.<br>Telephone No. 571-727-1600 |

Form PCT/IPEA/409 (cover sheet) (July 1998)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US04/18451

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☐ the international application as originally filed.
- ☒ the description:  
pages 1-26 as originally filed  
pages NONE filed with the demand  
pages NONE filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 27-28 as originally filed  
pages NONE as amended (together with any statement) under Article 19  
pages NONE filed with the demand  
pages NONE filed with the letter of \_\_\_\_\_.
- ☐ the drawings:  
pages NONE as originally filed  
pages NONE filed with the demand  
pages NONE filed with the letter of \_\_\_\_\_.
- ☐ the sequence listing part of the description:  
pages NONE as originally filed  
pages NONE filed with the demand  
pages NONE filed with the letter of \_\_\_\_\_.

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☐ The amendments have resulted in the cancellation of:**

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

**5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US04/18451**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

|                               |                                 |     |
|-------------------------------|---------------------------------|-----|
| Novelty (N)                   | Claims <u>8,9,18 and 19</u>     | YES |
|                               | Claims <u>1-7, 10-17, 20-21</u> | NO  |
| Inventive Step (IS)           | Claims <u>8-9, 18-19</u>        | YES |
|                               | Claims <u>1-7, 10-17, 20-21</u> | NO  |
| Industrial Applicability (IA) | Claims <u>1-21</u>              | YES |
|                               | Claims <u>NONE</u>              | NO  |

**2. CITATIONS AND EXPLANATIONS**

Claims 1-7, 10-17, and 20-21 lack novelty under PCT Article 33(2) as being anticipated by US 2002/0198216 A1, (Njoroge *et al.*) 26 December 2002.

Njoroge *et al.* teach pharmaceutical compositions and methods for treating tumors comprising administering an intracellular antagonist of the ras protein (para 0186) in combination with at least one signal transduction inhibitor (para 0190) wherein the signal transduction inhibitor is an epidermal growth factor receptor inhibitor or a HER2 receptor inhibitor (page 298). The epidermal growth factor receptor inhibitors specifically include intracellular or extracellular antagonists of EGFR such as IRESSA (ZD1939), OSI-774, cetuximab (Imclone C225), ABX-EGF, or herceptin (trastuzumab). The reference also teaches further administering an antineoplastic agent (page 297). Thus, the teachings broadly encompass a method of inhibiting a receptor tyrosine kinase (RTK) comprising administering an extracellular RTK antagonist (anti-EGFR antibodies) and an intracellular RTK antagonist.

Claims 1-6, 11-16, and 21 lack novelty under PCT Article 33(2) as being anticipated by US 2003/0073207 A1, (Akhtar *et al.*) 17 April 2003.

Akhtar *et al.* teach pharmaceutical compositions and methods for treating tumors comprising administering nucleic acids that target both EGFR and HER2 RNA (para 203) which encompasses administering an intracellular RTK antagonist. The reference further teaches administering monoclonal antibodies (IMC C22, and ABX-EGF) or specific tyrosine kinase inhibitors (OSI-774) and chemotherapy in combination with the nucleic acid inhibitors (para 207). See also pages 187-188.

Claims 8-9 and 18-19 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed invention.

Claims 1-21 meet the criteria set out in PCT Article 33(4), and thus meets industrial applicability because the subject matter claimed can be made or used in industry.